

REMARKS

This amendment responds to the Office Action dated 10/04/05, and follows the conference call interview that the co-inventor Yury and I had with you during the week of October 10. At that time, I was in Austin, TX on a cell phone and could not hear your responses fully. Only now, due to Yury's many business trips, have we been able to get together to prepare this response.

The invention teaches a stationary phase having a ligand comprised of both an ion-bearing functional group and a hydrophobic functional group (vis. long chain alkyl group), where the ligand is chemically bonded to a stationary support in a specifically arranged manner.

The pending amended Claim 8 thus relates to an improved stationary phase for adsorption chromatography, comprising ion bearing and hydrophobic functional groups that are connected together; where the ion bearing functional group is chemically attached directly to the rigid supporting material while the hydrophobic functional group is indirectly connected relative to the rigid supporting material surface via its connection to the ion bearing functional group; and further where the hydrophobic functional group has more than 4 carbon atoms forming a permeable stationary layer shielding said ion bearing functional group from full contact with the mobile phase.

This claimed arrangement is unique in adsorption chromatography, and Applicants' columns (SIELC or PRIMESEP) based on this technology have been both widely used and well received. To help establish this fact, and possibly even to

confirm that this technology is more than merely significant but possibly even semi-revolutionary, the undersigned invites the examiner to review relevant comments as posted on a chromatography forum web site, at:

[www.sepsci.com/chromforum/viewtopic.php?t=1479&start=0](http://www.sepsci.com/chromforum/viewtopic.php?t=1479&start=0)

Although all ligand arrangements of the references differ from the claimed combination, the rejection held that it would be obvious to change the formulations of these references, to optimize them. However, it would seem quite obvious to the undersigned, since the patent laws require that an applicant disclose the best mode of practicing the claimed invention, that each applicant at the time of his filing believed that his disclosure was the best for his respective type of separation.

One reference (Talley) specifically relates to exclusion chromatography that requires minimum interaction of analytes with a stationary phase surface. To achieve this need, the surface are made hydrophilic (vs. hydrophobic) and are positively charged to repel cationic polymers. Talley specifies that the alkyl substitutes on the ligand be no more than 4 carbon atoms long.

Talley neither disclosed nor suggested that a longer carbon chain (making it hydrophobic) would achieve any additional benefits in or toward adsorption chromatography. In fact, the Examiner is likely using the hindsight wisdom of Applicants' own disclosure as justification in holding that the claimed invention is but an obvious variation of Talley, although it has taken some thirty years to achieve this obvious(?) variation.

To highlight the unappreciated and unexpected benefits of this invention, note that material described by Talley is commercially available, and Fig. 8 in the subject

application shows a poor chromatogram obtained when using this material for separating a mixture of carboxylic acids. By contrast, a column made with material according to the current claim, with the same mobile phase mixture, produced the desirable widely separated component spikes of Fig. 7.

Applicant agrees with the examiner that the Snider classification indicated that both types of chromatography, absorption and size exclusion, can be identified as an HPLC or High Performance Liquid Chromatography. However, Claim 8 as now submitted is directed specifically to absorption chromatography HPLC, which is different from the size exclusion HPLC of Talley.

Ayers is directed to another type of chromatography, affinity separation. This type of separation is based on attachment of special ligand to the stationary phase which has high affinity to the analyte. This separation is based on recognition principle very specific toward unique molecules, primarily in the separation of bio-molecules, and otherwise is not in universal use.

O'Gara is directed to adsorption chromatography, which uses different materials than those disclosed herein, namely a polar group embedded within a hydrophobic stationary layer. However this embedded polar group is not ion-bearing, which is significantly different from the current invention. Thus, the O'Gara material would not interact with charged analytes, as the current invention does with its ion-exchange mechanism.

Figs. 11 and 12 again illustrate isolations of charged polar molecules (nucleosides), Fig. 11 illustrating successful separation using the combined ion exchange and RP mechanisms material of this invention compared to

unsuccessful separation of Fig. 12 using only the stationary phase materials of O'Gara.

Because several types of adsorption separations are possible due to dual functionality of the embedded ligand, the current invention provides a material with universal ramifications. Thus, the differing separations of reverse phase, normal phase, ion-exchange, and ion-exclusion are possible using columns having this claimed stationary phase material. The embedded polar groups like O'Gara are suitable only for reverse phase type of separation.

As noted, amended claim 8 recites that the stationary phase includes ion bearing and hydrophobic functional groups connected together, with only the ion bearing group being attached to the stationary phase support surface and with the hydrophobic functional group then being connected relative to the support surface, via its connection to the ion bearing functional group, and forming a permeable stationary layer shielding the ion bearing group from full contact with the related HPLC mobile phase.

The Talley molecular exclusion chromatography provides no attractive interaction between the stationary phase and solute, but molecular exclusion occurs due only to the size of molecules, the larger molecules passing through the stationary phase quicker than the smaller molecules. The Claim 8 adsorption separation stationary phase material provides for solute separation because of the attractive equilibration between the mobile and stationary phases; and the molecule size is of no concern. Talley limits the hydrocarbon chain to between one and four carbon units, while the claimed hydrophobic functional group is comprised as hydrocarbon chains of more than four carbon units. It cannot be obvious to "optimize" the Talley arrangement by

increasing the length of carbon chain to achieve the claimed arrangement, as in fact, "optimizing" Talley's restricted carbon chain would preclude a reliable size-exclusion process.

Ayers stationary phase utilized a hydrophobic group as a ligand, and O'Gara showed octadecyl and octyl groups as reverse phase ligands known for the past 30 years, forming the basis of the rejection that it would be obvious to use the traditional reverse phase ligands of the octadecyl and octyl groups in Ayers, believing further that this modified combination would function the same as the stationary phase of Claim 8.

However, this supposition is not true since the Ayers stationary phase connection of the ion bearing and hydrophobic functional groups is opposite to the claimed invention, whereby the Ayers hydrophobic group is bonded to the stationary phase surface and serves only as a flexible linkage in holding the ion bearing group relative to the stationary phase surface. Moreover, this hydrophobic group does not participate in any separation process.

By contrast, the hydrophobic group in the stationary phase invention of Claim 8 actively participates in the reverse phase separation; and having both ionic and hydrophobic functional groups arranged as claimed, makes possible dual interactive synergy of both hydrophobic and electrostatic separation forces.

Adding the O'Gara thirty year old technology of using octadecyl and octyl groups as traditional reverse phase ligands to the reversed orientation of the Ayers interconnected ion bearing and hydrophobic functional groups, would not yield the stationary phase recited in amended Claim 8. It further seems apparent that the thirty

year background of using related components would be strong evidence that the claimed invention is not obvious, but represents a significant invention over the cited prior art. In fact, this thirty year gap might suggest that the rejection of obviousness is based on applicants' own disclosure, rather than what the past showed or suggested.

Reconsideration of the rejection and acknowledgement that the disclosed invention is both novel and unexpected, and thus patentable is requested and believed in order.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Charles F. Lind".

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